Complete Summary

GUIDELINE TITLE

Evaluation and treatment of hirsutism in premenopausal women: an Endocrine Society clinical practice guideline.

BIBLIOGRAPHIC SOURCE(S)

Martin KA, Chang RJ, Ehrmann DA, Ibanez L, Lobo RA, Rosenfield RL, Shapiro J, Montori VM, Swiglo BA. Evaluation and treatment of hirsutism in premenopausal women: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab 2008 Feb 5; [159 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Hirsutism

GUIDELINE CATEGORY

Diagnosis
Evaluation
Prevention
Treatment

CLINICAL SPECIALTY

Endocrinology
Family Practice
Internal Medicine
Obstetrics and Gynecology

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To provide recommendations for the evaluation and treatment of hirsutism in premenopausal women

TARGET POPULATION

Premenopausal women with hirsutism

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis and Evaluation

Androgen level testing

Treatment

1. Pharmacologic therapy (monotherapy)
    - Oral contraceptive preparations (OCPs)
    - Antiandrogens (only recommended for women who cannot or choose not to conceive)
        - Flutamide and creams with antiandrogens were considered but not recommended
    - Glucocorticoids for women with hirsutism due to nonclassic congenital adrenal hyperplasia who have a suboptimal response to OCPs and/or antiandrogens, cannot tolerate them, or are seeking ovulation induction
    - Gonadotropin-releasing hormone (GnHR) in women with severe forms of hyperandrogenemia, such as ovarian hyperthecosis, who have a suboptimal response to oral contraceptive preparations and antiandrogens
    - Insulin-lowering drugs were considered but not recommended
2. Pharmacologic therapy (combination therapy)
    - Addition of an antiandrogen if patient-important hirsutism remains after 6 months of monotherapy
3. Direct hair removal methods
    - Laser/photoepilation with or without eflornithine cream
    - Laser/photoepilation in combination with pharmacologic therapy

MAJOR OUTCOMES CONSIDERED

- Severity of hirsutism scores

- Hair regrowth
- Patient well-being
- Side effects of treatment

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Quality of Evidence

High: ++++

Moderate: +++O

Low: ++OO

Very Low: +OOO

METHODS USED TO ANALYZE THE EVIDENCE

Meta-Analysis of Randomized Controlled Trials
Review of Published Meta-Analyses
Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Systematic reviews of available evidence were used to formulate the key treatment and prevention recommendations.

The document is analyzed by identifying the level of scientific evidence, rating it, and grading the recommendations using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) system. GRADE takes into

account relative strengths and weaknesses of the best available evidence to produce a thorough meta-analysis. These evidence-based reviews are coordinated by the Knowledge and Encounter Research workgroup at the Mayo Clinic College of Medicine.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Consensus was guided by systematic reviews of evidence and discussions during one group meeting, several conference calls, and e-mail communications. The drafts prepared by the Task Force with the help of a medical writer, were reviewed successively by The Endocrine Society's Clinical Guidelines Subcommittee (CGS), Clinical Affairs Core Committee (CACC), and Council.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Strong recommendations use the phrase "we recommend" and the number 1, and weak recommendations use the phrase "we suggest" and the number 2

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The version approved by the Clinical Guidelines Subcommittee (CGS), and Clinical Affairs Core Committee (CACC) was placed on The Endocrine Society's Web site for comments by members. At each stage of review, the Task Force received written comments and incorporated needed changes.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Definitions for the quality of the evidence (++++, +++O, ++OO, +OOO) and strength of recommendations (strong: 1, weak: 2) are provided at the end of the "Major Recommendations" field.

1.1. Diagnosis of hirsutism

1.1.1. We suggest against testing for elevated androgen levels in women with isolated mild hirsutism because the likelihood of identifying a medical disorder that would change management or outcome is low (2|+OOO).

1.1.2. We suggest testing for elevated androgen levels in women with (2|+OOO):

- Moderate or severe hirsutism
- Hirsutism of any degree when it is sudden in onset, rapidly progressive, or when associated with any of the following:
    - Menstrual irregularity or infertility
    - Central obesity
    - Acanthosis nigricans
    - Rapid progression
    - Clitoromegaly

2.0. Treatment of hirsutism in premenopausal women

2.0. For women with patient-important hirsutism despite cosmetic measures, we suggest either pharmacological therapy or direct hair removal methods (2|+OOO). The choice between these options depends on (a) patient preferences, (b) the extent to which the area of hirsutism that affects wellbeing is amenable to direct hair removal, and (c) access to and affordability of these alternatives.

2.1. Pharmacological treatments

2.1.1. Monotherapy

2.1.1.1. For the majority of women, we suggest oral contraceptives to treat patient-important hirsutism (2|+OOO); because of its teratogenic potential, we recommend against antiandrogen monotherapy unless adequate contraception is used (1|+OOO).

2.1.1.2. For women who cannot or choose not to conceive, we suggest the use of either oral contraceptive preparations (OCPs) or antiandrogens (2|+OOO). The choice between these options depends on patient preferences regarding efficacy, side effects, and costs.

2.1.1.3. We suggest against the use of flutamide therapy (2|+OOO).

2.1.1.4. We suggest against the use of topical antiandrogen therapy for hirsutism (2|+OOO).

2.1.1.5. We suggest against using insulin-lowering drugs as therapy for hirsutism (2|+OOO).

2.1.1.6. For women with hirsutism who do not have classic or nonclassic congenital adrenal hyperplasia due to 21-hydroxylase deficiency (CYP21A2), we suggest against glucocorticoid therapy (2|+OOO). We suggest glucocorticoids for women with hirsutism due to nonclassic congenital adrenal hyperplasia (NCCAH) who have a suboptimal response to oral contraceptive preparations (OCPs) and/or

antiandrogens, cannot tolerate them, or are seeking ovulation induction (2|+OOO).

2.1.1.7. We suggest against using gonadotropin-releasing hormone (GnRH) agonists except in women with severe forms of hyperandrogenemia, such as ovarian hyperthecosis, who have a suboptimal response to oral contraceptive preparations and antiandrogens (2|+OOO).

2.1.1.8. For all pharmacologic therapies for hirsutism, we suggest a trial of at least 6 months before making changes in dose, changing medication, or adding medication (2|+OOO).

2.1.2. Combination Therapy

2.1.2.1. If patient-important hirsutism remains despite 6 or more months of monotherapy with an oral contraceptive, we suggest adding an antiandrogen (2|++OO).

2.2. Direct hair removal methods

2.2.1. For women who choose hair removal therapy, we suggest laser/photoepilation (2|++OO). For women undergoing photoepilation therapy who desire a more rapid initial response, we suggest adding eflornithine cream during treatment (2|++OO). For women with known hyperandrogenemia who choose hair removal therapy, we suggest pharmacologic therapy to minimize hair regrowth (2|+OOO).

Definitions:

Quality of Evidence

High: ++++

Moderate: +++O

Low: ++OO

Very Low: +OOO

Strength of Recommendation

Strong: 1

Weak: 2

CLINICAL ALGORITHM(S)

A clinical algorithm is provided in the original guideline document on "Initial Evaluation of Hirsutism."

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of evidence supporting the recommendations is specifically stated for each recommendation.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate evaluation and treatment of hirsutism in premenopausal women for the reduction of hair growth and improved hirsutism scores

POTENTIAL HARMS

Antiandrogen Therapy

- Because of its teratogenic potential, antiandrogen monotherapy is recommended against unless adequate contraception is used.
- Spironolactone is generally well tolerated, but may have a dose-dependent association with menstrual irregularity unless an oral contraceptive preparation (OCP) is used concomitantly. It may rarely result in hyperkalemia, and it may cause an increased diuresis and occasionally postural hypotension and dizziness early in treatment. As with all antiandrogens, there is the danger of fetal male pseudohermaphroditism if used in pregnancy because of the exquisite sensitivity of the fetal genitalia to exposure to maternal synthetic sex hormone ingestion.
- Cyproterone acetate (CPA) is generally well tolerated, but there are dose-dependant metabolic effects similar to those of higher doses of oral contraceptives.

Glucocorticoid Therapy

Slight overdosing can occur even at recommended doses, and independent of daily or alternate-day administration, and may be associated with side effects, such as adrenal atrophy, increased blood pressure, weight gain, Cushingoid striae (particularly with dexamethasone), and decreased bone mineral density. Dehydroepiandrosterone-sulfate levels are used to indicate the degree of adrenal suppression; the target is a level of approximately 70 micrograms/dL.

GnRH Agonist Therapy

GnRHa therapy is expensive, requires injections, and, unless estrogen in some form is added, results in severe estrogen deficiency, with menopausal symptoms such as hot flashes, and bone loss. We therefore suggest not using GnRH agonists for most women with hirsutism.

Laser/Photoepilation Therapy

Laser/photoepilation hair removal: limitations include burning, pain, the need for multiple treatments, and the potential risk of dyspigmentation and scarring.

QUALIFYING STATEMENTS

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- Clinical Practice Guidelines are developed to be of assistance to endocrinologists by providing guidance and recommendations for particular areas of practice. The Guidelines should not be considered inclusive of all proper approaches or methods, or exclusive of others. The Guidelines cannot guarantee any specific outcome, nor do they establish a standard of care. The Guidelines are not intended to dictate the treatment of a particular patient. Treatment decisions must be made based on the independent judgment of healthcare providers and each patient's individual circumstances.
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IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Clinical Algorithm
Patient Resources

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Martin KA, Chang RJ, Ehrmann DA, Ibanez L, Lobo RA, Rosenfield RL, Shapiro J, Montori VM, Swiglo BA. Evaluation and treatment of hirsutism in premenopausal women: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab 2008 Feb 5; [159 references] PubMed

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2008 Feb

GUIDELINE DEVELOPER(S)

The Endocrine Society - Disease Specific Society

SOURCE(S) OF FUNDING

The Endocrine Society

GUIDELINE COMMITTEE

Hirsutism in Premenopausal Women Guideline Task Force

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Kathryn A. Martin, MD (Chair) – Significant Financial Interests: none declared; Governance: none declared; Consultation or Advisement: none declared; Grant or Other Research Support: none declared.

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**Evidence-based reviews for this guideline were prepared under contract with The Endocrine Society.*

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from The Endocrine Society Web site.

Print copies: Available from The Endocrine Society, c/o Bank of America, P.O. Box 630721, Baltimore, MD 21263-0736; Phone: (301) 941.0210; Email: Societyservices@endo-society.org

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

The following is available:

- The Hormone Foundation's patient guide to the evaluation and treatment of hirsutism in premenopausal women. Chevy Chase (MD): The Hormone Foundation. 2008 Apr. 2 p. Available from the Hormone Foundation Web site.

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC STATUS

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